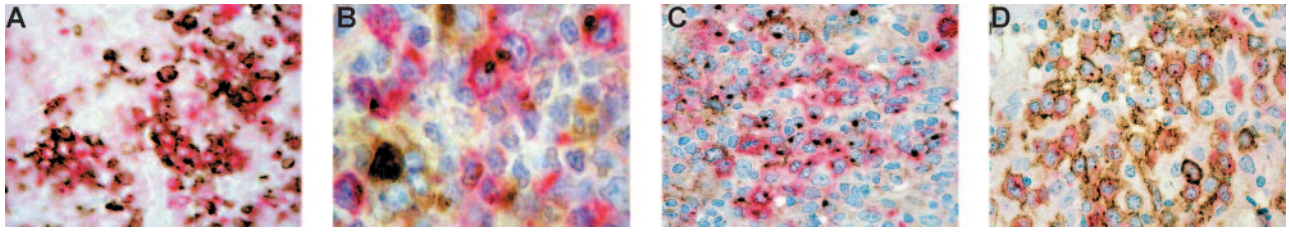

Figure 1. Activated follicular B helper T-cell phenotype of neoplastic cells in AITL. (A) Double immunostaining for CD10 in brown (DAB) and CXCL13 in red (Fast red TR) shows coexpression of CD10 and CXCL13 in tumor cells (no counterstain). (B) Double immunostaining for CXCL13 in red (Fast red TR) and CXCR5 in brown (DAB). The CXCL13$^+$ neoplastic cells display concomitant positivity for CXCR5. (C) Double immunostaining for CXCL13 in red (Fast red TR) and CD154 in brown (DAB) that demonstrates overlaying cytoplasmic staining in the neoplastic cells. (D) Double immunostaining for CD134 in brown (DAB) and CXCL13 in red (Fast red TR) shows coexpression of these 2 antigens in the neoplastic cells. Original magnifications, × 400 (A,C-D) and × 1000 (B). The double stainings were performed using EnVision-HRP (A,D) or CSA II System (B-C) in combination with EnVision-AP (A-D; all from DakoCytomation, Carpinteria, CA). Primary antibodies were as follows: polyclonal goat anti-CXCL13 (A-D) and monoclonal mouse anti-CXCR5 (B; R&D Systems, Minneapolis, MN); monoclonal mouse anti-CD10 (A), anti-CD154 (C), and anti-CD134 (D; Novocastra Laboratories, Newcastle upon Tyne, United Kingdom). Images were visualized on a Nikon Eclipse E600 microscope equipped with a Nikon Plan 40 ×/0.65 objective or 100 ×/1.25 oil-immersion objective lens; images were then captured via a Nikon Coolpix 4500 digital camera and processed with Adobe PhotoShop 7.0 software (Adobe Systems, San Jose, CA).

expression of CXCL13 and CXCR5 in neoplastic T cells, again pointing to a T_{FH} phenotype.[3-8] Coexpression of the CXCR5 chemokine receptor and its ligand CXCL13 suggests an autocrine loop, possibly contributing to the survival of neoplastic T cells. All cases demonstrated coexpression of CD154 in the majority of the neoplastic T cells. This antigen plays a crucial role in GC formation[9] and provides survival signals to follicular B cells.[6] Each case showed significant but variable numbers (10%-100%) of CXCL13$^+$ T cells bearing CD134, whose expression on activated CD4$^+$ T cells either initiates their migration into or causes them to be retained in B follicles.[10] One case coexpressed CD57 in a significant proportion of neoplastic cells, while the remaining cases displayed only a minute fraction of CD57$^+$CXCL13$^+$ cells that may reflect the residual normal T_{FH} cells. Since proliferating FDCs expressed CXCL13 and are known to express CD40[9] (receptor for CD154) and OX40L[6,10] (ligand for CD134), our data suggest a selective cross-talk between FDCs and neoplastic T cells.

Our observations not only fully support the notion of Grogg et al[1] but extend it by a more detailed analysis, establishing that the phenotype of the neoplastic cells (as shown here) is consistent with activated T_{FH} cells localized at the boundary between the mantle zone and the GC light zone.[6] These findings provide direct explanations for some peculiar features of AITL, including B-cell hyperactivation and hypergammaglobulinemia despite gradual reduction of follicular B-cell mass, as well as the follicular outgrowths of FDCs as a result of stimulation by neoplastic T_{FH} cells. Further investigations will be needed to explain loss of follicular B cells, a phenomenon that occurs in advanced cases and may be caused by a disarranged dialogue between neoplastic T_{FH} cells and nonneoplastic B cells.

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To the editor:

Immune thrombocytopenic purpura does not exhibit a disparity in prevalence between African American and white veterans

Ethnic, racial, and geographic differences influence virtually all human disease, and certain conditions exhibit well-established differences between Africans and Europeans.[1] Once such differences are identified, it is important to examine them, because etiologic, genetic, and therapeutic heterogeneity may be present.[2,3] In addition, ethnic disparities of all types may be accompanied by

Table 1. Characteristics of the study cohort: white and African American male veterans with at least one hospital admission between July 1, 1969, and September 30, 1996, who were followed more than 1 year

Characteristics	Whites		African Americans	
	Other than ITP	ITP	Other than ITP	ITP
No. of subjects	3 882 044	5 939	873 265	1257
Mean age at study entry, y*	51.8	52.2	47.4	47.8
Years of follow-up (mean)†	11.6	5.5	11.9	6.0
Person-y at risk†	45 214 080	32 525	10 374 274	7484
Mean age at ascertainment of ITP, y	NA	58.7	NA	54.8

ITP indicates immune thrombocytopenic purpura (applied ICD-8 code: 287.1, ICD-9 code: 287.3); and NA, not applicable.
*Age at first discharge record for inpatient hospitalization at Veterans Affairs hospitals between July 1, 1969, and September 30, 1996.
†The first year of follow-up was censored.

important social differences influencing medical access or diverse cultural practices with consequences for health care delivery and outcomes. It is therefore crucial to confirm conclusions about putative racial disparities with well-grounded assessments derived from large population–based data to avoid erroneous conclusions.

A recent review of previous small studies[4-10] reported that the proportion of African American patients with immune thrombocytopenic purpura (ITP) was very low compared with the proportion of African Americans in the population. If that is the case, further investigation of environmental, social, and genetic factors that contribute would be a priority. However, if the report is not valid, not only will such investigations be fruitless, but negative social, economic, and public health consequences could result; for example, the level of suspicion for ITP in African Americans might be inappropriately low.

The cohort was identified from discharge records for inpatient hospitalizations at 142 nationwide Veterans Affairs (VA) hospitals between July 1, 1969, and September 30, 1996.[11] The target population for calculation of ITP prevalence included all African American (N = 874 522) and white (N = 3 887 983) male veterans hospitalized at least once at age 18 or older (Table 1).

Age-adjusted prevalence rates were directly standardized to the adult year 2000 United States standard population. Approval for these studies was obtained from the institutional review board of the National Institutes of Health (NIH). Informed consent was waived because we had no contact with study subjects.

We identified 1257 cases of ITP in African Americans and 5939 in whites (Table 1). Mean age at study entry for African American and white patients with ITP was 47.8 and 52.2 years, respectively. The age-adjusted prevalence for ITP was 189.3 (153.7-224.9, 95% confidence interval [CI]) per 100 000 for African Americans and 176.4 (161.5-191.3, 95% CI) per 100 000 for whites. The corresponding age-adjusted prevalence rate for ITP was 1.1-fold (0.9-1.3, 95% CI) higher in African Americans than in whites; the difference was not significant.

Our results indicate a similar age-adjusted prevalence of ITP among African Americans who were diagnosed in the hospital compared with whites and are in sharp contrast with previous small ITP studies.[4-10] Our study's strengths include its large size (n = 7196) in a patient population with relatively stable and standardized access to medical care that is provided to veterans independent of ethnicity or socioeconomic status. Limitations include lack of detailed individual patient data, possible confounding due to differential utilization of services by race, and retrospective design derived from hospital discharge records, which potentially could bias our observations, since ITP usually does not lead to hospitalization. Since ITP is thought to be predominant in women, the restriction to male sex might limit the generalizability of our results. The varying specificity of applied ICD (International Classification of Diseases) codes over the 30-year study period would have resulted in inclusion of some subjects with thrombocytopenia other than ITP. However, the age-adjusted prevalence of ITP was assessed among African Americans and whites using the same hospital discharge registry, and such variations should be nondifferential between the 2 races.

In conclusion, we found little evidence of disparity in ITP prevalence among African American and white veterans.

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O.L. and G.G. designed the study and obtained data; O.L., G.G., and T.R.F. analyzed data; all authors were involved in the interpretation of the results; O.L. initiated this work and wrote the report; all authors read, gave comments, and approved the final version of the manuscript; and all authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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